

Remarks

Claims 1, 4, 7-12, 23 and 28-33 are before the Examiner.

The Examiner's remarks in the Office Action are addressed below.

Claim Rejections Under U.S.C. § 103(a)

Claims 1, 4, 7-12, 23 and 28-33 stand rejected under 35 U.S.C. 103(a) based on the Examiner's contention that they are obvious over Guley et al., (U.S. Patent No. 4,309,405) in view of Jain et al., (U.S. Patent No. 4,610,870). The Examiner asserts that Guley et al. teaches a composition comprising both water soluble and water insoluble polymers, in particular, plural water soluble polymers including hydroxypropyl methyl cellulose (HPMC) and hydroxypropyl cellulose (HPC) and plural water-soluble polymers including ethylcellulose (EC) and carboxyvinyl cellulose. The Examiner also asserts that Jain et al. teaches the equivalence of HPC and hydroxyethyl cellulose (HEC) in the core.

The Applicants respectfully disagree with the Examiner.

Guley et al. relates to a sustained release composition with a core formulation that comprises "about 20% to about 70% by weight of the core of the drug or drugs for which sustained release is desired, and about 30% to about 72% by weight of the core of the water soluble polymer(s) and the water insoluble polymer mixture" (Column 2, lines 27-31). The water soluble polymer can be at least one of HPMC and HPC (Column 2, lines 40-43) and the water insoluble polymer mixture is EC or EC and at least one of carboxyvinyl polymer, hydroxypropyl methylcellulose phthalate (HPMCP) and HPC (Column 2, lines 45-50). Guley et al. does not specifically teach or suggest the use of a combination of HPMC and HEC.

Jain et al. relates to a controlled release formulation containing a core portion. The core portion contains a medicament and one or more water-soluble or water-swellaable hydrocolloid gelling agents. It is described at column 5, lines 21-35, of Jain et al. that the hydrocolloid "preferably comprise cellulose polymers which are cellulose ethers such as methyl cellulose, cellulose alkyl hydroxylates such as HPMC, HPC, HMC or HEC, cellulose alkyl carboxylates such as carboxymethyl cellulose and carboxyethyl cellulose, and alkali metal salts of cellulose

alkyl carboxylates, such as sodium carboxymethyl cellulose and sodium carboxyethyl cellulose, as well as carboxypolymethylene (molecular weight 2.5 to 3.5 million). Preferred are sodium carboxymethyl cellulose, methyl cellulose, HPMC and carboxypolymethylene" (emphasis added). Applicants had previously argued in the response dated November 6, 2003 that Jain et al. does not teach the equivalency of cellulose alkyl hydroxylates. Jain et al. simply lists examples of these compounds, which does not, on its' own, teach the equivalency of these compounds. The Examiner asserts that a listing of these compounds in the alternative indicates that any one of them can be substituted for another in the list. Applicants agree that, in accordance with Jain et al.'s controlled release formulation, one may choose from a list of cellulose alkyl hydroxylates but this does not enable one skilled in the art to conclude that such compounds are equivalent and interchangeable for the same purpose. In fact, Applicants' submit that cellulose derivatives are not equivalent and, consequently, not interchangeable for the same purpose. This is supported by the data in the Declaration (signed November 4, 2003) attached hereto as Attachment 1, which was previously submitted to the U.S. Patent and Trademark Office on January 8, 2004. For example, the data showed that the amount of drug released in 1 hour is 17% for HPMC, 60% for HEC and 88% for EC. The time taken for 70% of the drug (i.e., $T_{70\%}$) to be released was about 9 hours for HPMC, 4 hours for HEC and 30 minutes for EC. These results clearly indicate that HPMC, HEC and EC are neither equivalent nor interchangeable for the same purpose. Therefore, it cannot be concluded that cellulose derivatives are equivalent and interchangeable for the same purpose.

In fact, Applicants have provided a further Declaration signed June 8, 2004 showing a comparison of the specific combination of HEC/HPMC of the claimed invention versus HPC/HPMC attached hereto as Attachment 2. The results shown in Table 2 and Figure 1 of the Declaration show significant differences between the release profiles of the two formulations. The amount of drug released in 1 hour is 38% for the HPC/HPMC combination, while the amount of drug released in 1 hour is only 28% for the HEC/HPMC combination. The difference between the two combinations increases with time. For example, the amount of drug released in 4 hours is greater than 90% for the HPC/HPMC combination, while the amount of drug released in 4 hours is less than 70% for the HEC/HPMC combination. Furthermore, it takes 5 hours to release 100% of the drug for the HPC/HPMC combination, while it takes 8 hours before 100% of

the drug is released for the HEC/HPMC combination. These results show significant differences in the effect of drug release and availability of the two formulations and clearly indicate that HEC and HPC are not equivalent and interchangeable when used in combination with HPMC. The differences between the two formulations can impact the decision as to how often a product ought to be taken daily in order to be effective, which also impacts on patient compliance and wellness. These differences also impact adverse effects or safety especially for high potency drugs with low therapeutic indices.

Based on these submissions, the Applicants respectfully submit that an HPC/HPMC combination is not equivalent to an HEC/HPMC combination and, therefore, respectfully request withdrawal of the 35 U.S.C. § 103(a) rejection of the present claims.

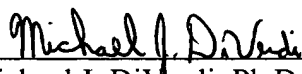
Conclusion

In view of the above amendments and remarks, the Applicants believe that the pending claims are in condition for allowance. If a telephone conversation with Applicant's attorney would expedite prosecution of the application, the Examiner is urged to contact the undersigned.

Respectfully submitted,

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